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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,066	05/08/2001	Chris Small	263/204	3766

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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	6

DATE MAILED: 04/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/852,066	SMALL ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Information Disclosure Statement

The information disclosure statement filed 5/8/01 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each reference listed that is not in the English language. The IDS has been placed in the application file, but references AH, AI, AJ, AM, and AP have not been considered. None of the references are in English, have an English language abstract, or are accompanied by an English language translation. No statement of relevance, or recitation of the reference in the specification has been found by the examiner for any of these references. As no explanation of relevance for any of the references designated AH, AI, AJ, AM or AP has been filed, these references have not been considered. The examiner's signature on the IDS indicates that only the initialed references have been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites comparison of a measured phospholipid concentration to a "normal concentration". The term "normal concentration" may have several meanings in

the art; e.g. the concentration found in a normal subject, an average or mean concentration found in a population (but not necessarily in a single "normal" subject), the concentration in the same subject prior to developing a disorder or disease, or prior to administration of a medicament, etc. As it is unclear what meaning applicant intends for the phrase "normal concentration", the claims are indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11, 13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of UEDA *et al.* (IDS ref: US 5,122,454) and GILLETT *et al.* (IDS ref: Atherosclerosis (1975) vol. 22, pp. 111-124).

Claim 1 recites a method to detect a disease condition by digesting a phospholipid in a sample of bodily fluid with a first enzyme to produce a substrate, then subjecting the substrate to a second enzyme in an enzyme cycling reaction to produce a detectable product, calculating the concentration of phospholipid by measuring the amount of product, correlating that concentration to the disease condition by comparison to a "normal" concentration. Claim 2 limits the first enzyme to lysophospholipase, phospholipase B, phospholipase A_1, or phospholipase A_2. Claim 3 limit the second enzyme to a specific list. Claim 4 limits the substrate to glycerol-3-phosphate. Claims 5 and 6 limit the detectable product to hydrogen peroxide and the measuring step to hydrogen peroxide accumulation. Claims 7 and 8 limit the detectable product to NADH and the measuring step to measurement of NADH oxidation. Claim 9 limits the enzyme cycling reaction to reacting glycerol-3-phosphate with glycerol-3-pohosphate dehydrogenase and glycerol-3-phosphate oxidase. Claim 10 limits the bodily fluid. Claim 11 limits the method to further comprise extracting lipids from the sample of bodily fluid. Claim 13 limits the method to one wherein an increase or decrease in phospholipid concentration compared to concentrations from normal subjects indicates a disease condition. Claim 15 limits the disease to a blood disorder.

UEDA teaches measurement of lysolecithin (LPC, a phospholipid) in serum using a combination of enzymes, including lysophospholipase, G3P dehydrogenase, G3P oxidase, NADH, and measurement of G3P as a detectable product by measuring oxidation of NADH (col. 11, lines 10-43). UEDA further teaches that phospholipase A_2 may be used in his assay (col. 11, lines 45-47), teaches that his G3P reactions are

cycling reactions (col. 5, lines 45-61), and teaches measurement of an increase in hydrogen peroxide by colorimetry (col. 6, lines 33-41). UEDA does not teach a correlation between an altered phospholipid level and a disease condition such as a blood disorder.

GILLETT teaches a method of correlating heart disease or peripheral arterial disease with decreased levels of lysolecithin (LPC) in test subjects as compared to normal (healthy) subjects (pp. 111, 117, and 119).

It would have been obvious to one of ordinary skill in the art at the time of invention to have included the enrichment step of GILLETT in the method of measuring LPC of UEDA where the motivation would have been to remove possibly interfering contaminants from the sample. In addition, it would have been obvious to have combined the correlation of heart and arterial disease with decreased LPC levels with the method of measuring LPC as taught by UEDA where the motivation would have been to correlate a colorimetric measurement of LPC with a disease condition by measuring G3P produced in the method of UEDA. One skilled in the art would reasonably have expected success in using the method of UEDA to measure LPC in a method for detecting (i.e. correlating to) a disease condition, such as that of GILLETT, because UEDA teaches that his method of measuring G3P produced from LPC can be used in methods correlating levels of a compound to disease conditions (abstract).

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of MILLS et al. (WO 98/43093) and UEDA *et al.* (IDS ref: US 5,122,454).

The claims recite a method of detecting a disease condition by measuring the concentration of phospholipids in a sample of bodily fluid, as set forth above. Claim 12 limits the method to one wherein the comparing step comprise comparing the concentration of phospholipid to an earlier concentration from the same subject. Claim 14 limits the disease to gynecological or ovarian cancer.

MILLS teaches a method of detecting cancer, specifically ovarian or gynecological cancer, by measuring the concentration of LPC (LysoPC) and lysophosphatidic acid (LysoPA) in a sample of bodily fluid (p. 8), comparing the concentration(s) to that from normal subjects and determining that a subject has a disease if the concentrations differ (abstract and pp. 3-4). MILLS teaches that that the concentrations of phospholipids may be measured over time (i.e. one measurement may be compared to an earlier measurement from the same subject, p. 5), and teaches that lipids may be extracted from the sample of bodily fluid before measurement of phospholipids, wherein the amount of phospholipid may be quantified by biochemical assays using enzymes (p. 14, lines 8-18). MILLS teaches a variety of bodily fluids (p. 12, lines 31-32) which may be used in his method. MILLS does not teach a cycling reaction nor the specific enzymes recited in the claims.

UEDA teaches a method of measuring LPC using a cycling reaction and lysophospholipase and/or phospholipase A_2, as set forth above.

It would have been obvious to one of ordinary skill in the art at the time of invention to have used the enzymatic reactions taught by UEDA to quantitate the phospholipids in the method of MILLS where the motivation would have been to

facilitate detection of a disease by using a sensitive colorimetric or fluorescent assay to measure LP levels in a bodily fluid by measuring the amount of G3P produced, as suggested by UEDA. One skilled in the art would have expected success in measuring the phospholipids of MILLS using the enzymes of UEDA because both teach measurement of LPC in bodily fluids, the LPA of MILLS is known in the art to react with lysophospholipase, MILLS teaches that enzymatic reactions may be used for quantitation in his method, and UEDA teaches that at least LPC can be successfully measured using his enzyme reactions.

Double Patenting

Claims 1-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15, respectively, of U.S. Patent No. 6,248,553. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '53 patent differ from the instant claims only in that claim 1 of '553 recites digesting lysophosphatidic acid, which is a species of phospholipid, whereas instant claim 1 recites digestion of phospholipids (the genus). A species anticipates a genus (see MPEP 2131.02), therefore the claims of '553 render the claims of the instant application obvious.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Conclusion

Claims 1-15 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER
Marjorie A. Moran
4/14/03